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Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

Sub-Committee of Experts on the Transport of Dangerous Goods

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Item 3 of the provisional agenda
Listing, classification and packing

Revised OECD Test Guideline 431 allowing sub-categorisation for skin corrosion

Transmitted by the European Union*

Introduction

1. OECD Test Guideline (TG) 431 "In vitro Skin Corrosion: Human Skin Model Test" was updated to introduce sub-categorisation for skin corrosion and adopted by the OECD in 2013 and further revised in 2014, 2015 and 2016, as TG 431 "In vitro skin corrosion: reconstructed human epidermis (RHE) test method". The in vitro methods included in TG 431 can now discriminate between GHS sub-category 1A and sub-category 1B/C. Discrimination between skin corrosive sub-categories 1B and 1C was not possible to introduce, due to the limited set of well-known in vivo corrosive sub-category 1C chemicals against which to validate the in vitro method results.

2. The main reason to introduce sub-categorisation in TG 431 was to avoid general classification in GHS category 1, which probably would inspire further in vivo testing to rule out a category 1A (corresponding to packing group I in transport of dangerous goods regulations).

* In accordance with the programme of work of the Sub-Committee for 2017-2018 approved by the Committee at its eighth session (see ST/SG/AC.10/C.3/100, paragraph 98 and ST/SG/AC.10/44, paragraph 14)

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3. The categorisation referred to is based on the classification criteria set out in the GHS, Rev. 7 (Table 3.2.1):

	Criteria
Category 1	Destruction of skin tissue, namely, visible necrosis through the epidermis and into the dermis, in at least one tested animal after exposure ≤ 4 h
Sub-category 1A	Corrosive responses in at least one animal following exposure ≤ 3 min during an observation period ≤ 1 h
Sub-category 1B	Corrosive responses in at least one animal following exposure > 3 min and ≤ 1 h and observations ≤ 14 days
Sub-category 1C	Corrosive responses in at least one animal after exposures > 1 h and ≤ 4 h and observations ≤ 14 days

4. The corresponding assignment of packing groups in the UN Model Regulations Rev. 20, is described in Table 2.8.3.4 for Class 8, corrosive substances:

Packing Group	**Exposure Time**	**Observation Period**	**Effect**
I	≤ 3 min	≤ 60 min	Irreversible damage of intact skin
II	> 3 min ≤ 1 h	≤ 14 d	Irreversible damage of intact skin
III	> 1 h ≤ 4 h	≤ 14 d	Irreversible damage of intact skin
III	-	-	Corrosion rate on either steel or aluminium surfaces exceeding 6.25 mm a year at a test temperature of 55°C when tested on both materials

5. According to the GHS, corrosive substances should be classified in Category 1 where sub-categorisation is not required by the competent authority or where data is not sufficient. The sub-categorisation is not usually implemented by any competent authority because of use-and-supply concern, as skin contact should be avoided for all substances classified as corrosive (Category 1). The GHS sub-classification is rather originating from the necessity to assign different packing groups to guarantee safe transport. For skin corrosion the packing group I, II and III corresponds to GHS sub-category 1A, 1B and 1C.

6. The OECD Guidance Document No. 203 "*New Guidance Document on an Integrated Approach on Testing and Assessment (IATA) for skin corrosion and irritation*" states at the end of page 28, the following:

> *"OECD TG 431 also allows for the sub-categorisation of corrosive chemicals into Cat. 1A or Cat. 1B-and-1C but does not permit the distinction of the latter into Cat. 1B and Cat. 1C. It is important to note however that the protocol and prediction model of the EpiSkinTM test method permits subcategorization of corrosive chemicals into the three Categories 1A, 1B and 1C, but its ability to discriminate between Categories 1B and 1C was never formally evaluated/validated due to the lack of high quality reference in vivo data against which to benchmark the in vitro results (Fentem et al. 1998, Alépée et al. 2014a). This method may in some cases nevertheless be considered for this purpose before any in vivo testing is performed if the result 1B or1C is considered in a weight of evidence approach (see Modules 5a,*

below). If this is not possible a cautious default classification as 1B if OECD TG431 results in 1B/1C could be decided."

7. For safe transport it makes a major difference if the substance is in packing group I compared II/III. However the difference if a substance is classified in packing group II or III is usually of less concern. It is therefore suggested, based on the revision of TG 431, to make it possible to classify in packing group I based on TG431, and in case it is not possible to discriminate between packing group II and III based on TG 431, allow for classification in packing group II rather than perform further *in vivo* testing. It could also be considered to apply the EpiSkinT^{M} results to distinguish between packing group II and III, as mentioned above.

Proposal

8. Based on this discussion, the relevant text from the UN Model Regulations Rev. 20 could be revised as follows (stricken out text is deleted, bold italized text is added):

"2.8.3.2 In assigning the packing group in accordance with 2.8.2.3, account shall be taken of human experience in instances of accidental exposure. In the absence of human experience the grouping shall be based on data obtained from experiments in accordance with OECD Test Guideline 404[1], ~~or~~ 435[2] ***or 431[34]. If it is not possible to discriminate between packing groups II and III in TG 431, packing group II can be applied.*** A substance or mixture which is determined not to be corrosive in accordance with OECD Test Guideline 430[3] ~~[4]~~ ~~or 431[4]~~ may be considered not to be corrosive to skin for the purposes of these Regulations without further testing.

[1] OECD Guideline for the testing of chemicals No. 404 "Acute Dermal Irritation/Corrosion" 2015

[2] OECD Guideline for the testing of chemicals No. 435 "In Vitro Membrane Barrier Test Method for Skin Corrosion" 2015

[3] OECD Guideline for the testing of chemicals No. 431 "In Vitro Skin Corrosion: reconstructed human epidermis (RHE) test method" 2016

[34] *OECD Guideline for the testing of chemicals No. 430 "In Vitro Skin Corrosion: Transcutaneous Electrical Resistance Test (TER)" 2015*

~~*[4] OECD Guideline for the testing of chemicals No. 431 "In Vitro Skin Corrosion: Human Skin Model Test" 2015*~~".